

Supplementary Note: Assessment of TumorBoost based on  
tumor/normal pair TCGA-23-1027 in the Affymetrix  
GenomeWideSNP\_6 data set TCGA,OV,Birdseed,ismpolish  
using the SNPs with 90% highest confidence scores

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# 1 Introduction

This report, which is automatically generated, assesses the performance of the TumorBoost method based on a few change points in a particular tumor/normal pair. For more details on the evaluation methods, see the main TumorBoost manuscript.

## 2 Data set

The evaluation is this report is based on the tumor/normal pair (01A,10A) for individual TCGA-23-1027 in the data set TCGA,OV,Birdseed,ismpolish.

### 2.1 Preprocessing methods

The data was generated on the Affymetrix GenomeWideSNP\_6 chip type.

There is one CEL file per hybridization. The CEL files were preprocessed using Birdseed/median polish Korn *et al.* (2008) as part of a larger batch of CEL files.

### 2.2 Stratification on genotype confidence scores

We focus on the SNPs in which we are the most confident that they are heterozygous: the evaluation will involve the 90% SNPs with highest genotype confidence scores.

### 2.3 List of change points

For this data set, we have selected a few regions for which one can safely assume that there exists a single copy number change point. By definition, each change point separates two sets of genomic loci such that the true Decrease in Heterozygosity (DH) is the same within one set of loci but differs between the two sets. These regions were selected visually. For each region we chose a large enough safety margin to make our evaluation independent of the uncertainty on the true location of the change point.

Chr	Region	Change point	Margin	Before	After
2	108-140	124	0.5	'normal' (1,1)	'gain' (1,2)
2	125-157	141	0.5	'gain' (1,2)	'copy neutral LOH' (0,2)
10	80-109	94	0.5	'normal' (1,1)	'deletion' (0,1)
10	106.5-113.5	110	0.5	'deletion' (0,1)	'copy neutral LOH' (0,2)
2	55-75	65	0.5	'normal' (1,1)	'gain' (1,2)

Table 1: Regions in TCGA-23-1027 used for the evaluation and that each contain a single changepoint. All positions and lengths are in units of Mb.

We next compare how well each of these change points is detected using the above preprocessed signals followed or not by TumorBoost normalization using the ROC analysis described in the main TumorBoost manuscript at the full resolution as well as smoothed resolution with bin sizes  $h = \{1, 2, 4\}$ . Specifically, we compare the following three methods: (1) “**raw**”: preprocessed signals without TumorBoost normalization. (2) “**TBN,Birdseed**”: preprocessed signals followed by TumorBoost normalization using Birdseed genotype calls. (3) “**TBN,NGC**”: preprocessed signals followed by TumorBoost normalization using NGC genotype calls. For completeness we also include an evaluation of Total copy numbers (TCN).

### 3 Region: TCGA-23-1027:Chr2@108-140,cp=124+/-0.5,s=0/1

#### 3.1 Decrease in Heterozygosity (DH) and total copy-number tracks

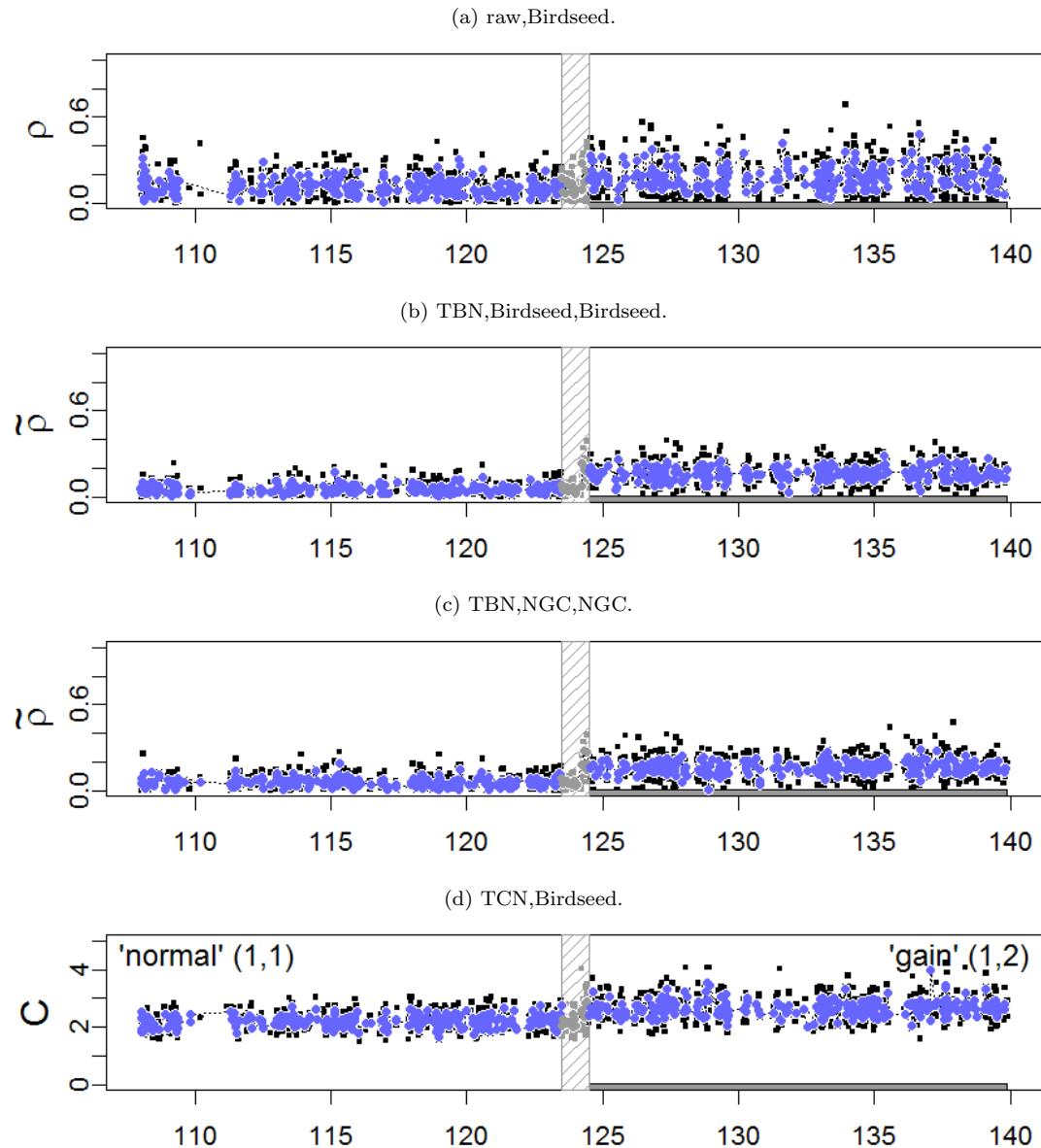


Figure 1: Decrease in Heterozygosity (DH) and total copy numbers for region TCGA-23-1027:Chr2@108-140,cp=124+/-0.5,s=0/1. Only heterozygous SNPs are plotted. There are 1056 loci of state 'normal' (1,1) ("negatives") and 1056 loci of state 'gain' (1,2) ("positives"), where the latter are highlighted with a solid bar beneath. In total 72 loci within the safety margin were excluded.

### 3.2 Allele B fraction density plots

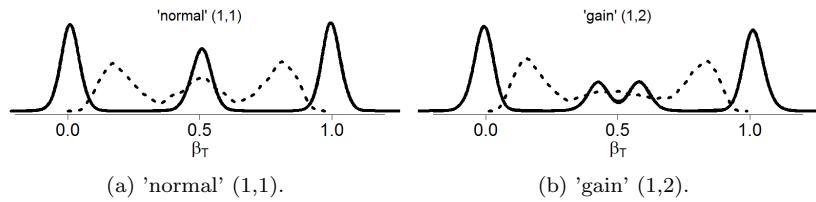


Figure 2: Density of raw (dashed lines) and TumorBoost-normalized (solid lines) allele B fractions for region TCGA-23-1027:Chr2@108-140,cp=124+/-0.5,s=0/1.

### 3.3 ROC curves

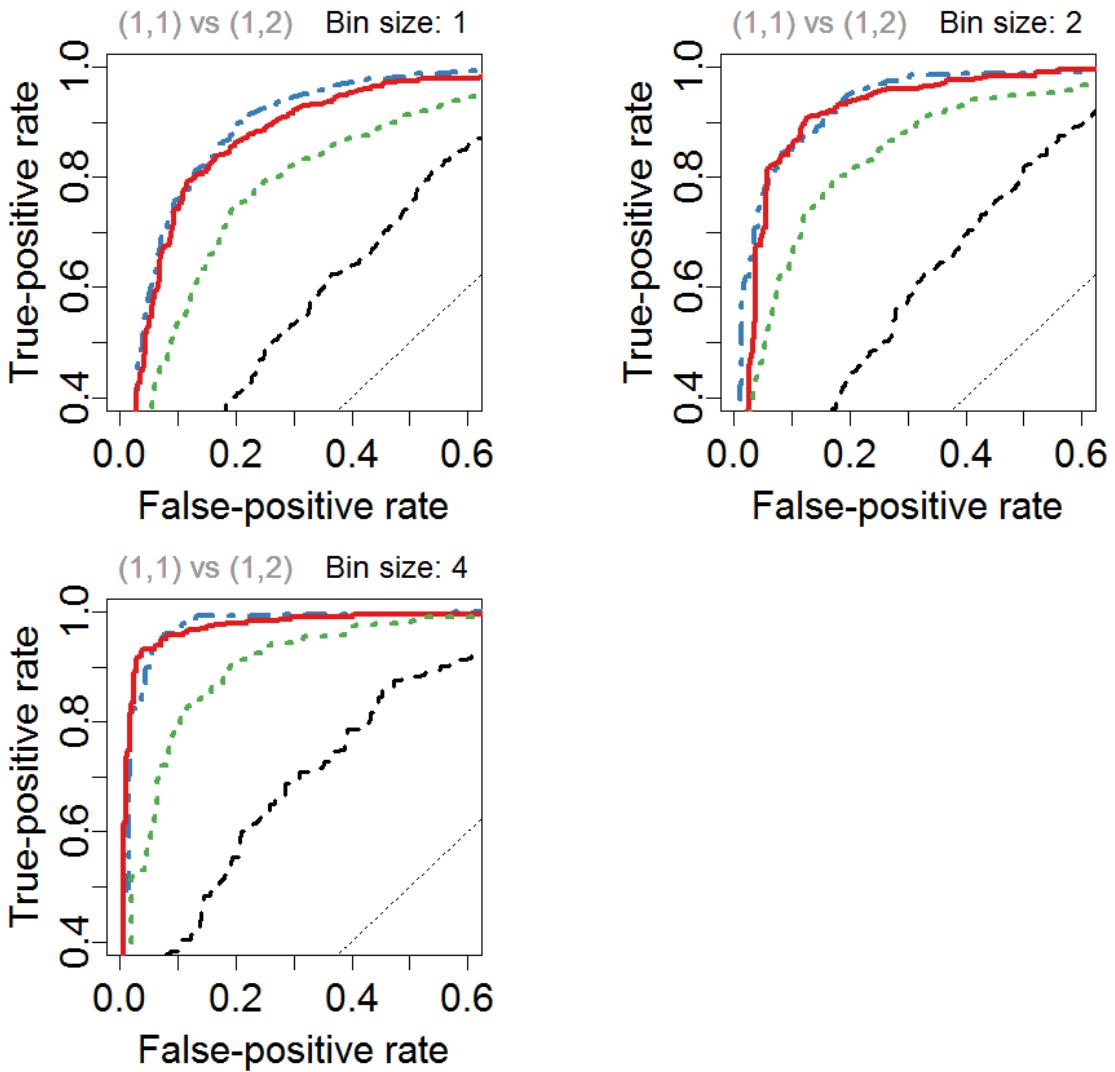


Figure 3: ROC curves for each preprocessing method at the full resolution as well as 2 different amounts of smoothing (using the `mean()` function) for region TCGA-23-1027:Chr2@108-140,cp=124+/-0.5,s=0/1. Legend: raw,Birdseed (dashed; `#000000`), TBN,Birdseed,Birdseed (dash-dotted; `#377EB8`), TBN,NGC,NGC (solid; `#E41A1C`) and TCN,Birdseed (dotted; `#4DAF4A`).

### 3.4 $(\beta_N, \beta_T)$ plots

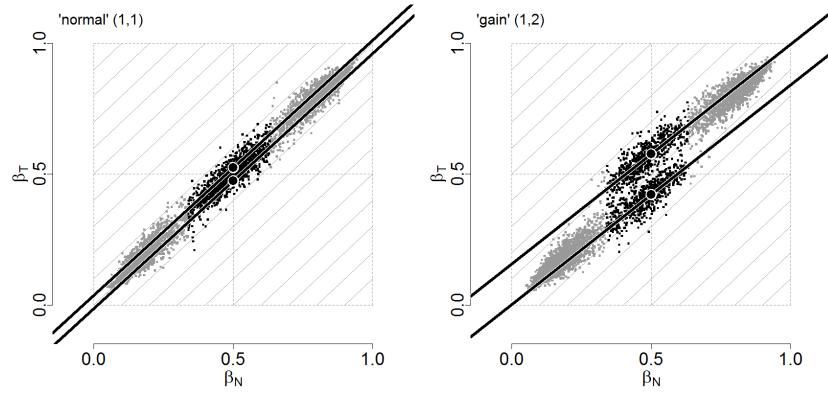


Figure 4: raw,NGC for region TCGA-23-1027:Chr2@108-140,cp=124+/-0.5,s=0/1.

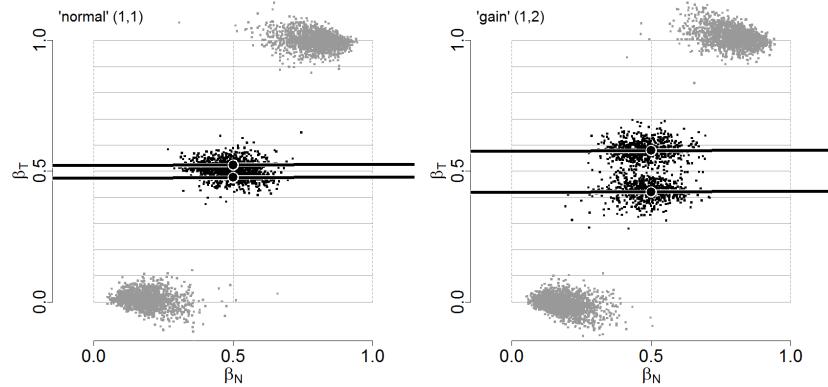


Figure 5: TBN,Birdseed,Birdseed for region TCGA-23-1027:Chr2@108-140,cp=124+/-0.5,s=0/1.

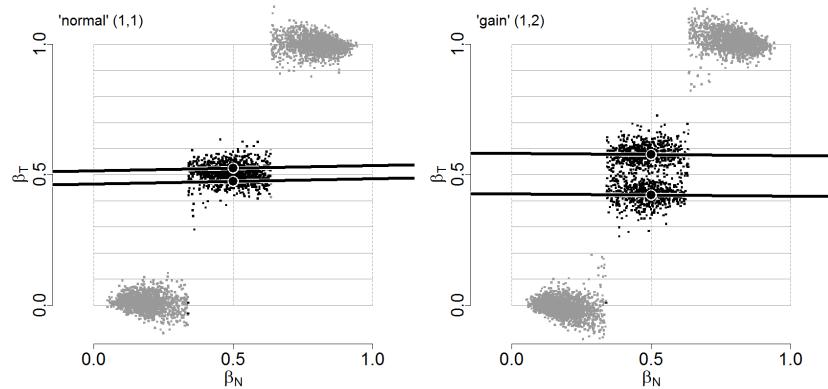


Figure 6: TBN,NGC,NGC for region TCGA-23-1027:Chr2@108-140,cp=124+/-0.5,s=0/1.

### 3.5 Allele-specific copy number estimates

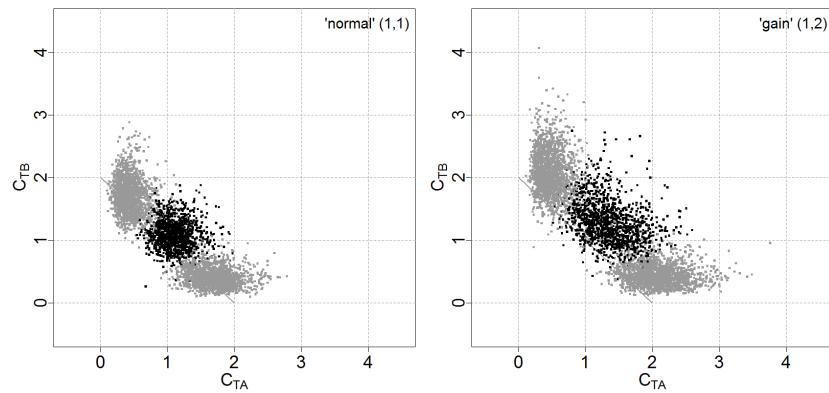


Figure 7: raw,NGC for region TCGA-23-1027:Chr2@108-140,cp=124+/-0.5,s=0/1.

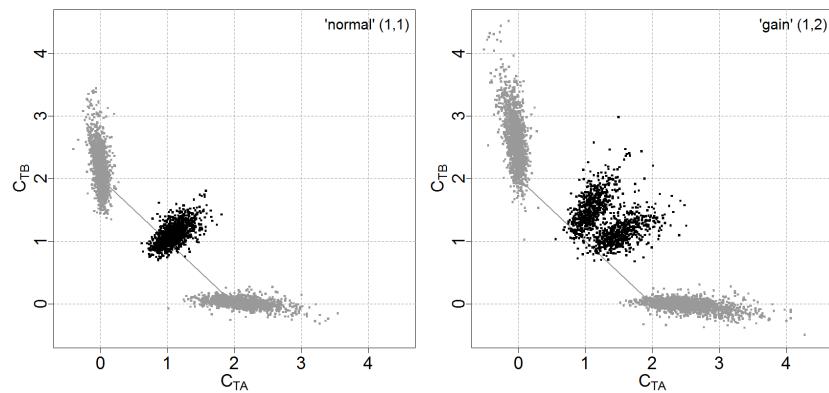


Figure 8: TBN,Birdseed,Birdseed for region TCGA-23-1027:Chr2@108-140,cp=124+/-0.5,s=0/1.

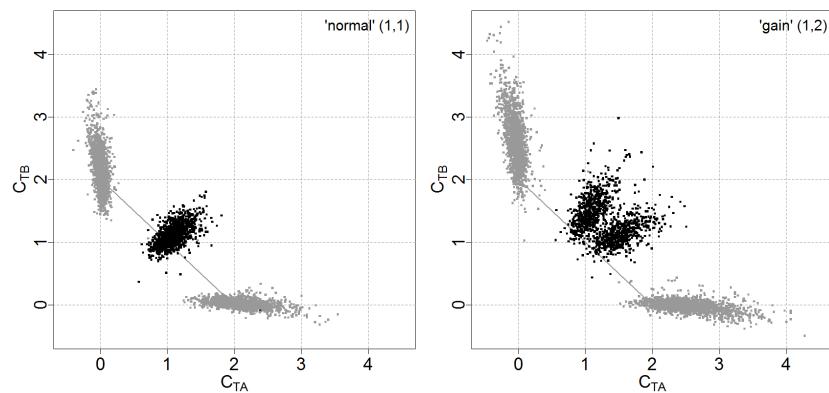


Figure 9: TBN,NGC,NGC for region TCGA-23-1027:Chr2@108-140,cp=124+/-0.5,s=0/1.

## 4 Region: TCGA-23-1027:Chr2@125.0-157.0,cp=141.0+/-0.5,s=1/3

### 4.1 Decrease in Heterozygosity (DH) and total copy-number tracks

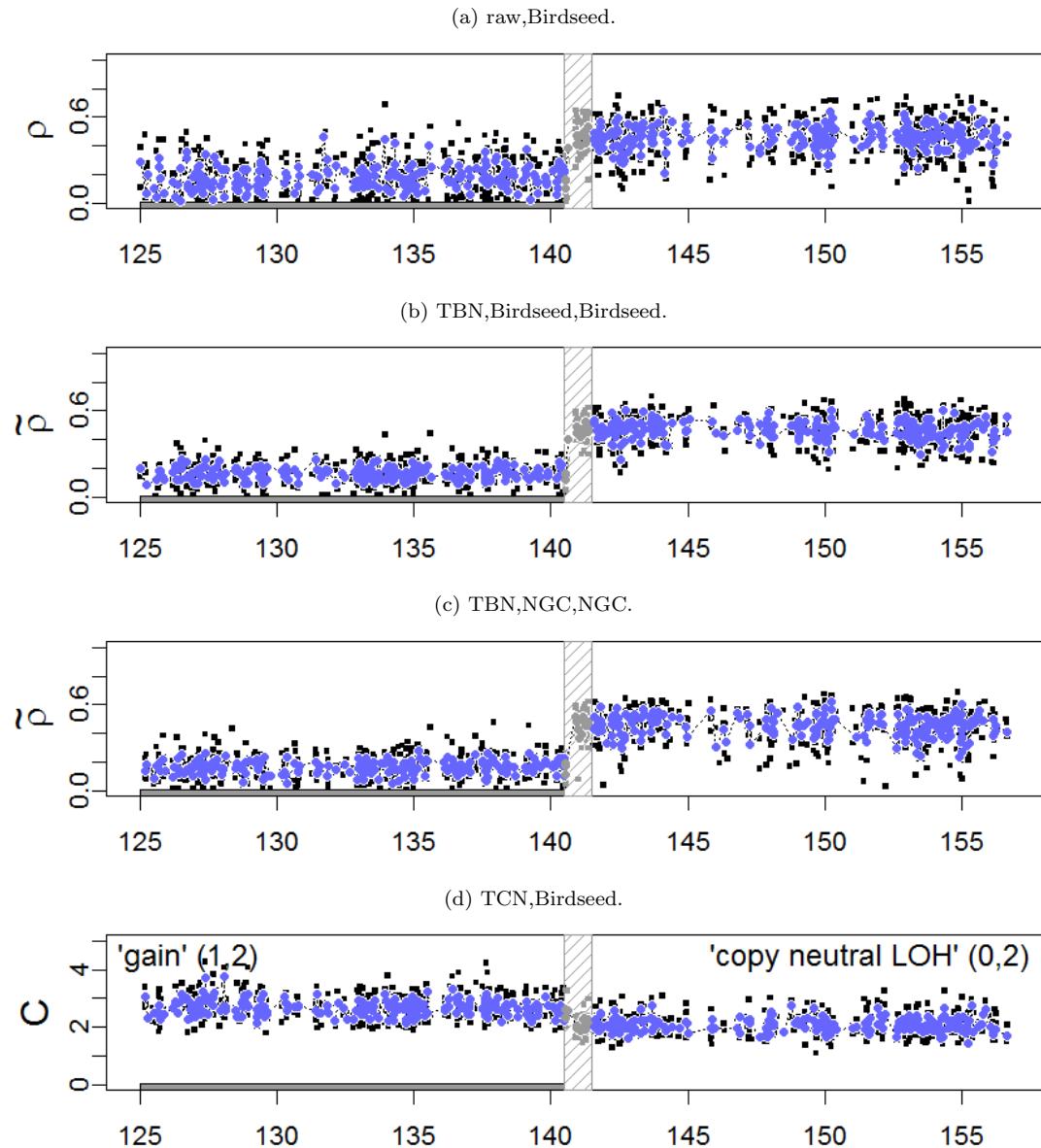


Figure 10: Decrease in Heterozygosity (DH) and total copy numbers for region TCGA-23-1027:Chr2@125.0-157.0,cp=141.0+/-0.5,s=1/3. Only heterozygous SNPs are plotted. There are 907 loci of state 'gain' (1,2) ("negatives") and 907 loci of state 'copy neutral LOH' (0,2) ("positives"), where the latter are highlighted with a solid bar beneath. In total 60 loci within the safety margin were excluded.

## 4.2 Allele B fraction density plots

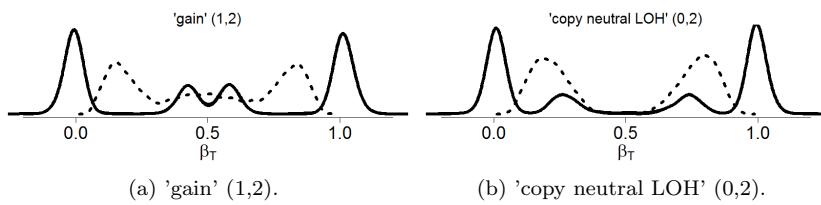


Figure 11: Density of raw (dashed lines) and TumorBoost-normalized (solid lines) allele B fractions for region TCGA-23-1027:Chr2@125.0-157.0,cp=141.0+/-0.5,s=1/3.

### 4.3 ROC curves

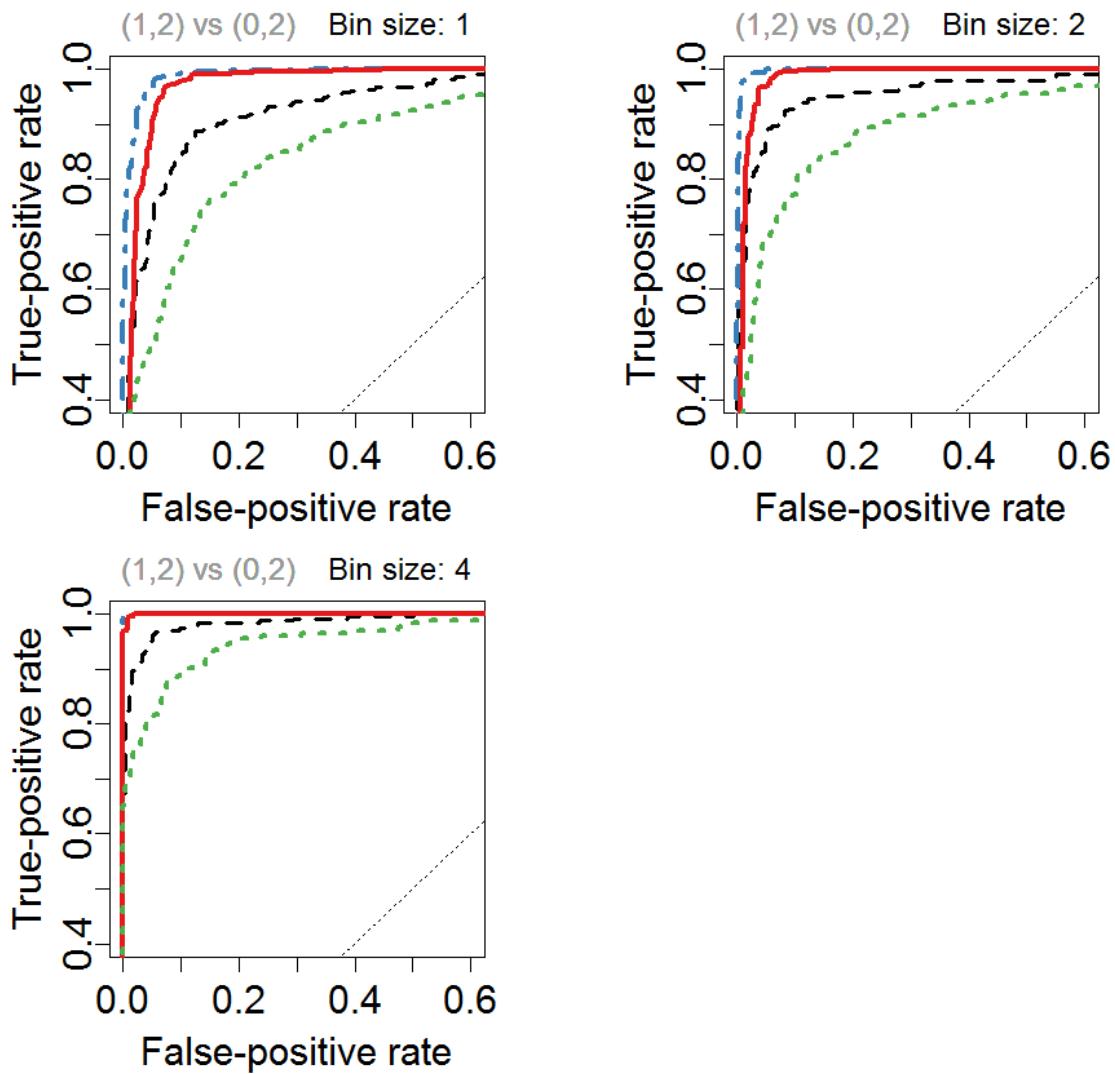


Figure 12: ROC curves for each preprocessing method at the full resolution as well as 2 different amounts of smoothing (using the mean() function) for region TCGA-23-1027:Chr2@125.0-157.0,cp=141.0+-0.5,s=1/3. Legend: raw,Birdseed (dashed; #000000), TBN,Birdseed,Birdseed (dash-dotted; #377EB8), TBN,NGC,NGC (solid; #E41A1C) and TCN,Birdseed (dotted; #4DAF4A).

#### 4.4 $(\beta_N, \beta_T)$ plots

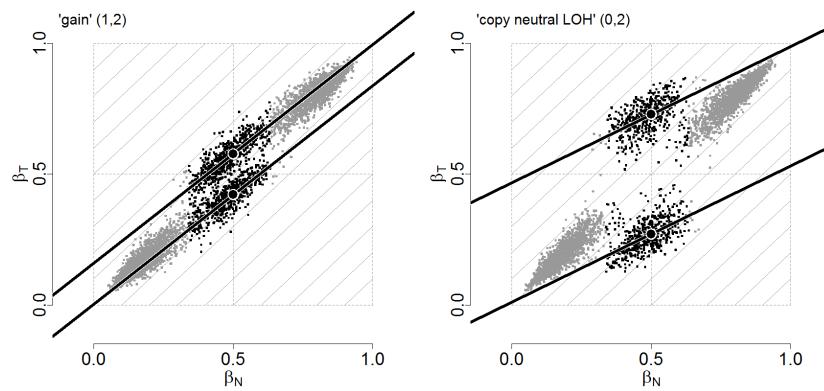


Figure 13: raw,NGC for region TCGA-23-1027:Chr2@125.0-157.0,cp=141.0+/-0.5,s=1/3.

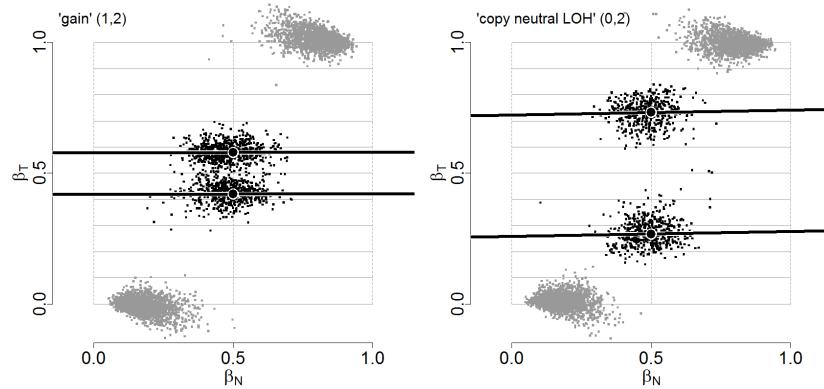


Figure 14: TBN,Birdseed,Birdseed for region TCGA-23-1027:Chr2@125.0-157.0,cp=141.0+/-0.5,s=1/3.

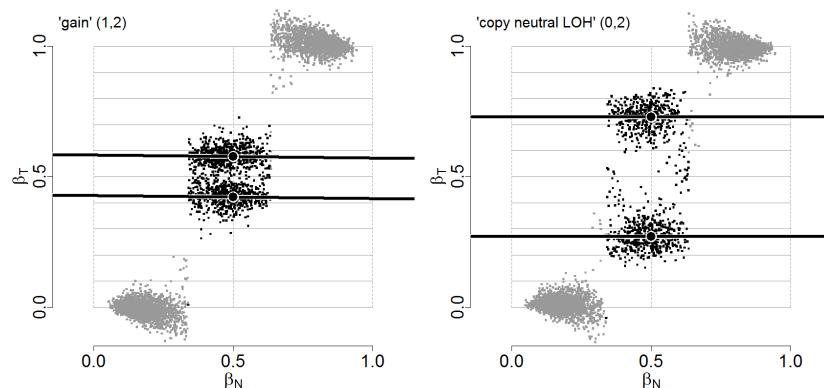


Figure 15: TBN,NGC,NGC for region TCGA-23-1027:Chr2@125.0-157.0,cp=141.0+/-0.5,s=1/3.

#### 4.5 Allele-specific copy number estimates

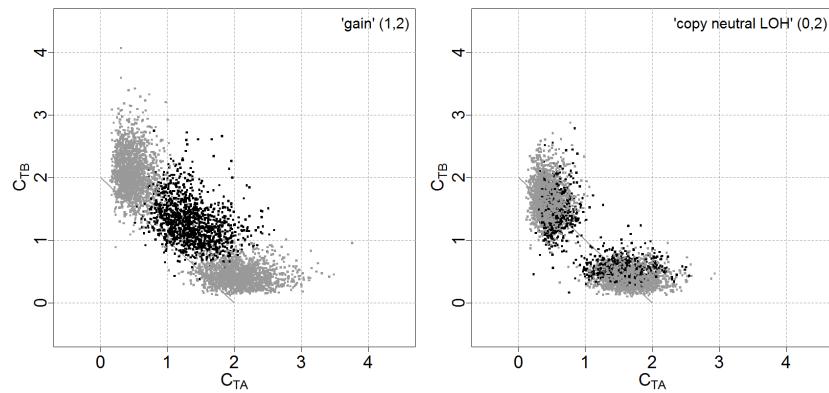


Figure 16: raw,NGC for region TCGA-23-1027:Chr2@125.0-157.0,cp=141.0+/-0.5,s=1/3.

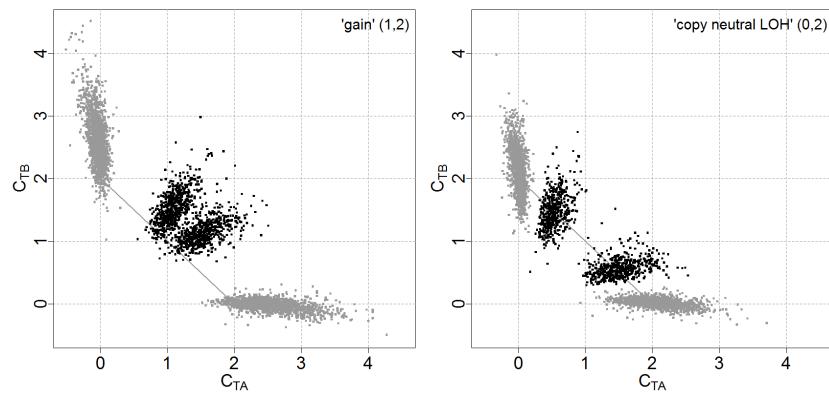


Figure 17: TBN,Birdseed,Birdseed for region TCGA-23-1027:Chr2@125.0-157.0,cp=141.0+/-0.5,s=1/3.

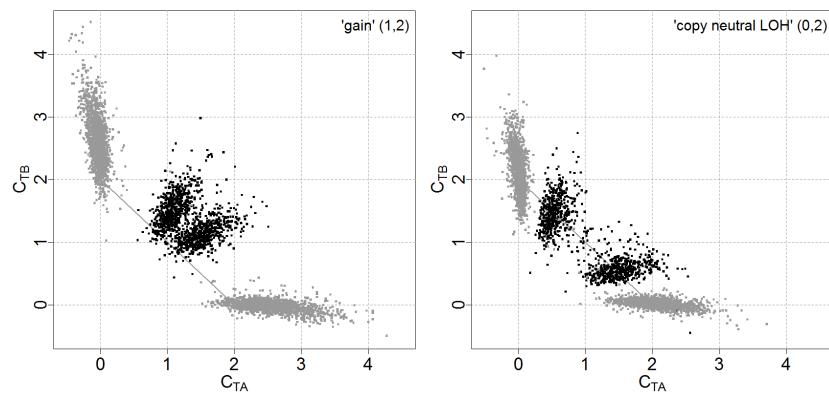


Figure 18: TBN,NGC,NGC for region TCGA-23-1027:Chr2@125.0-157.0,cp=141.0+/-0.5,s=1/3.

## 5 Region: TCGA-23-1027:Chr10@80-109,cp=94+/-0.5,s=0/2

### 5.1 Decrease in Heterozygosity (DH) and total copy-number tracks

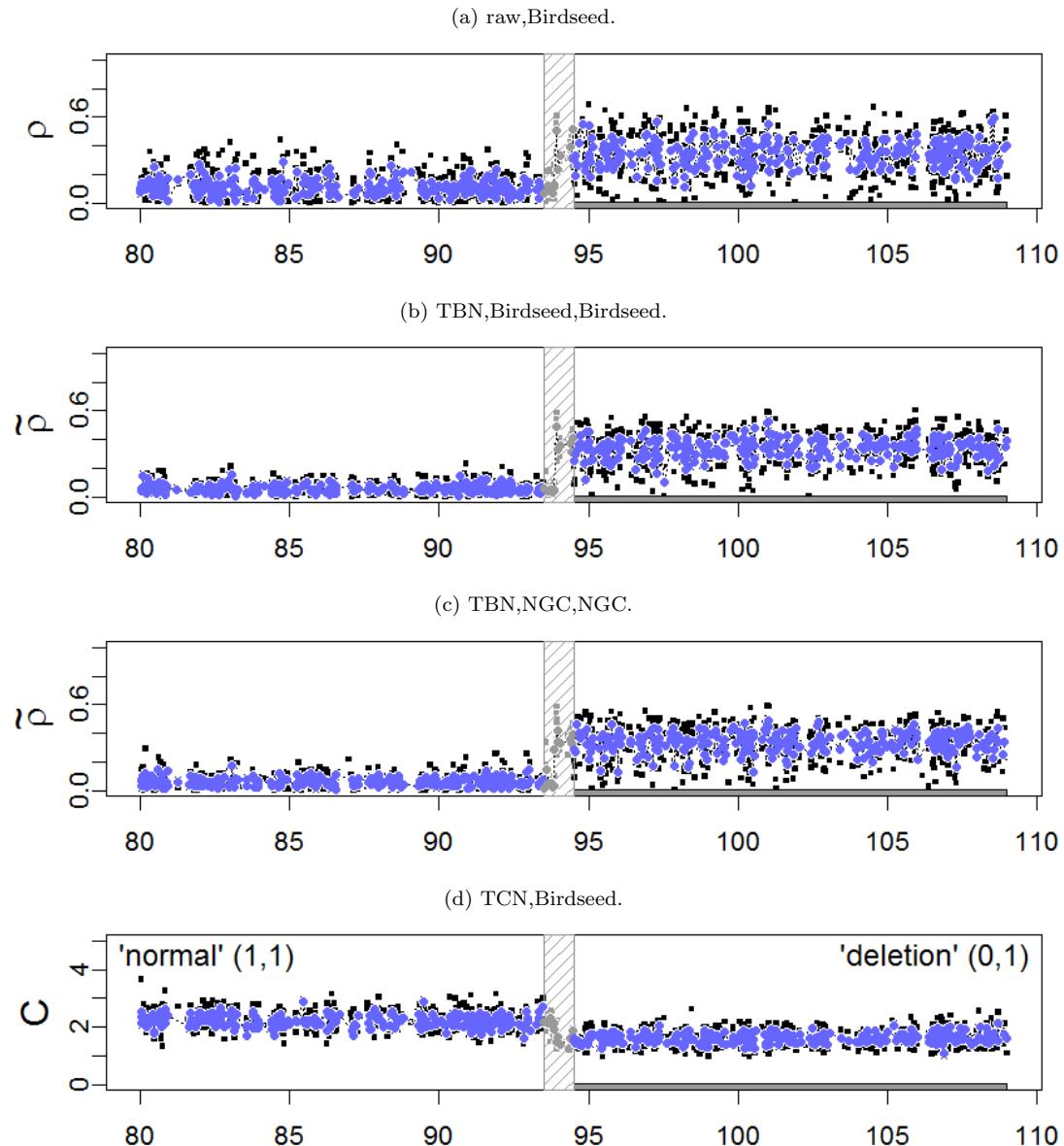


Figure 19: Decrease in Heterozygosity (DH) and total copy numbers for region TCGA-23-1027:Chr10@80-109,cp=94+/-0.5,s=0/2. Only heterozygous SNPs are plotted. There are 1132 loci of state 'normal' (1,1) ("negatives") and 1132 loci of state 'deletion' (0,1) ("positives"), where the latter are highlighted with a solid bar beneath. In total 47 loci within the safety margin were excluded.

## 5.2 Allele B fraction density plots

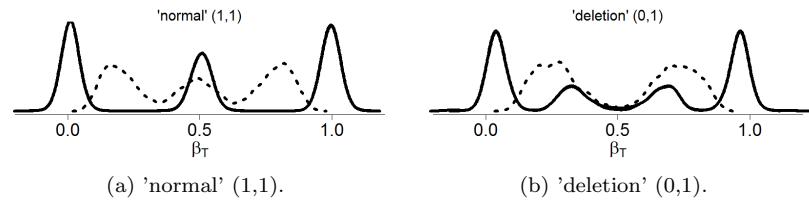


Figure 20: Density of raw (dashed lines) and TumorBoost-normalized (solid lines) allele B fractions for region TCGA-23-1027:Chr10@80-109,cp=94+/-0.5,s=0/2.

## 5.3 ROC curves

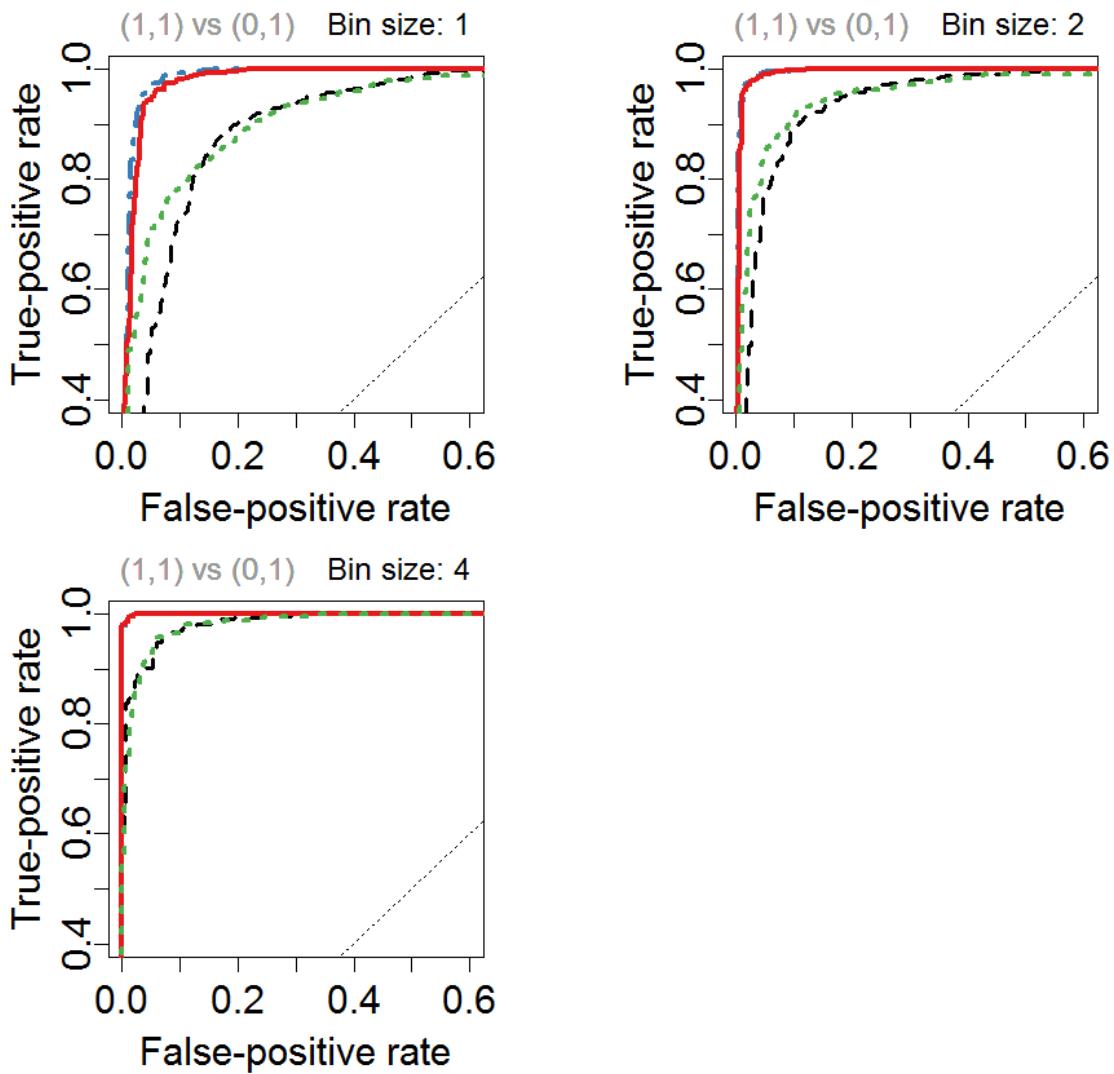


Figure 21: ROC curves for each preprocessing method at the full resolution as well as 2 different amounts of smoothing (using the `mean()` function) for region TCGA-23-1027:Chr10@80-109,cp=94+/-0.5,s=0/2. Legend: raw,Birdseed (dashed; `#000000`), TBN,Birdseed,Birdseed (dash-dotted; `#377EB8`), TBN,NGC,NGC (solid; `#E41A1C`) and TCN,Birdseed (dotted; `#4DAF4A`).

## 5.4 $(\beta_N, \beta_T)$ plots

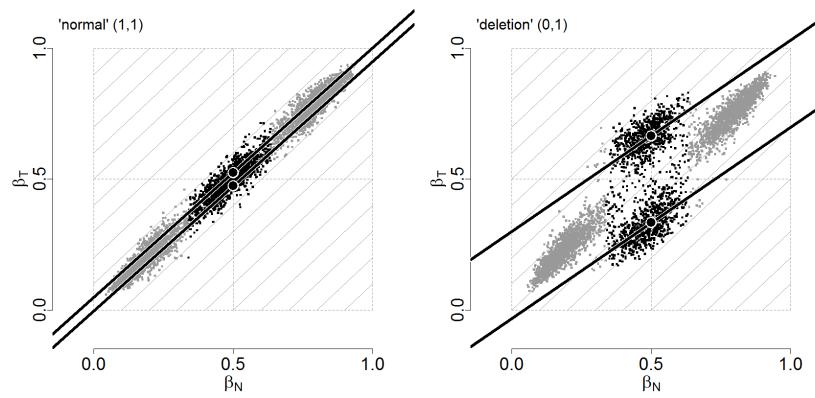


Figure 22: raw,NGC for region TCGA-23-1027:Chr10@80-109,cp=94+/-0.5,s=0/2.

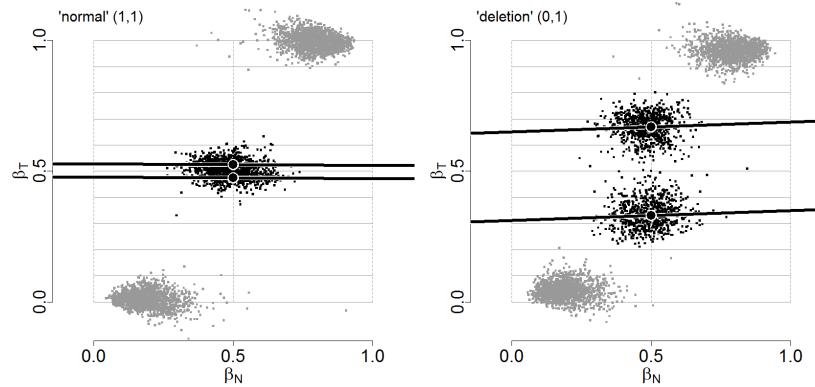


Figure 23: TBN,Birdseed,Birdseed for region TCGA-23-1027:Chr10@80-109,cp=94+/-0.5,s=0/2.

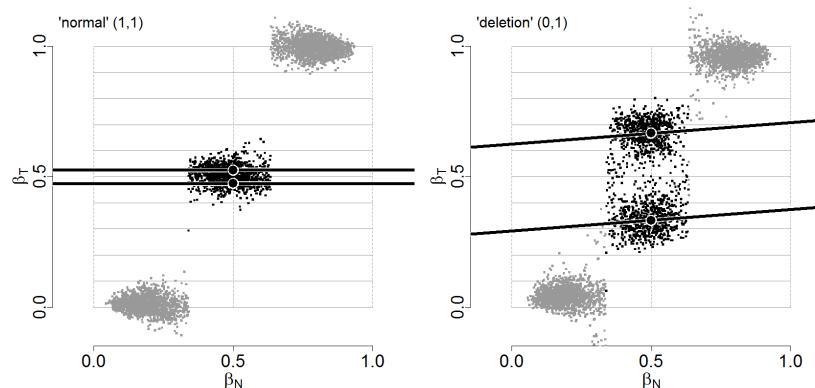


Figure 24: TBN,NGC,NGC for region TCGA-23-1027:Chr10@80-109,cp=94+/-0.5,s=0/2.

## 5.5 Allele-specific copy number estimates

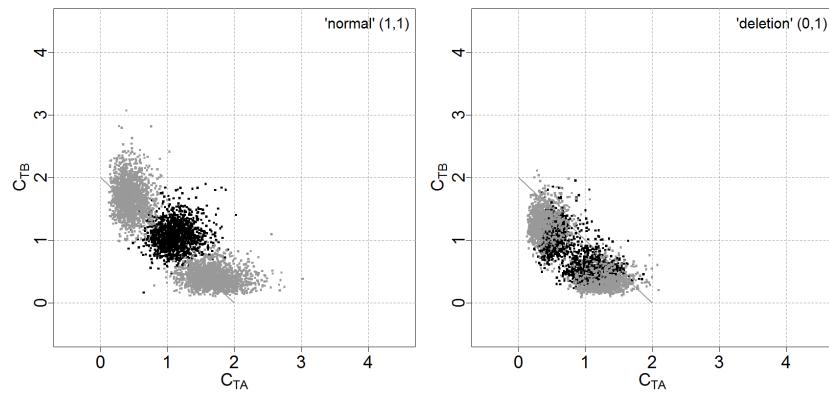


Figure 25: raw,NGC for region TCGA-23-1027:Chr10@80-109,cp=94+/-0.5,s=0/2.

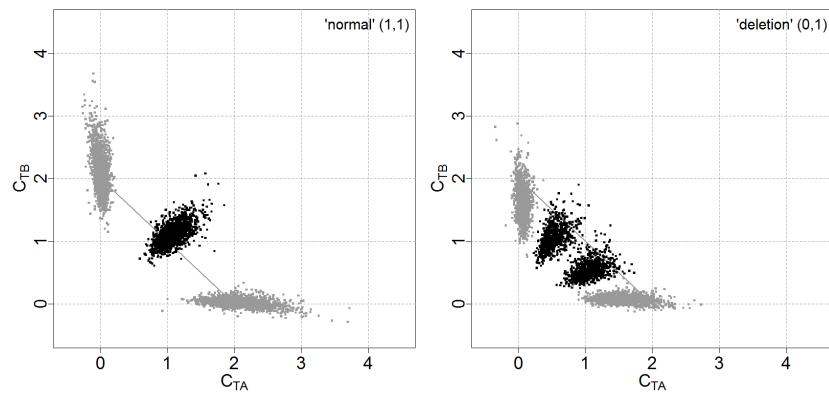


Figure 26: TBN,Birdseed,Birdseed for region TCGA-23-1027:Chr10@80-109,cp=94+/-0.5,s=0/2.

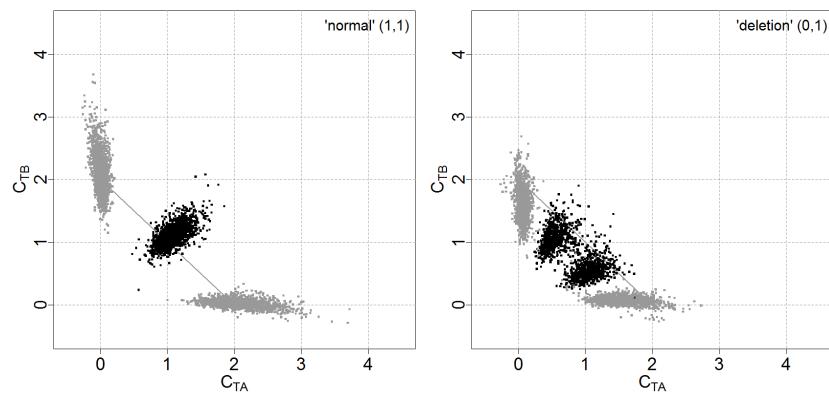


Figure 27: TBN,NGC,NGC for region TCGA-23-1027:Chr10@80-109,cp=94+/-0.5,s=0/2.

## 6 Region: TCGA-23-1027:Chr10@106.5-113.5,cp=110+/-0.5,s=2/3

### 6.1 Decrease in Heterozygosity (DH) and total copy-number tracks

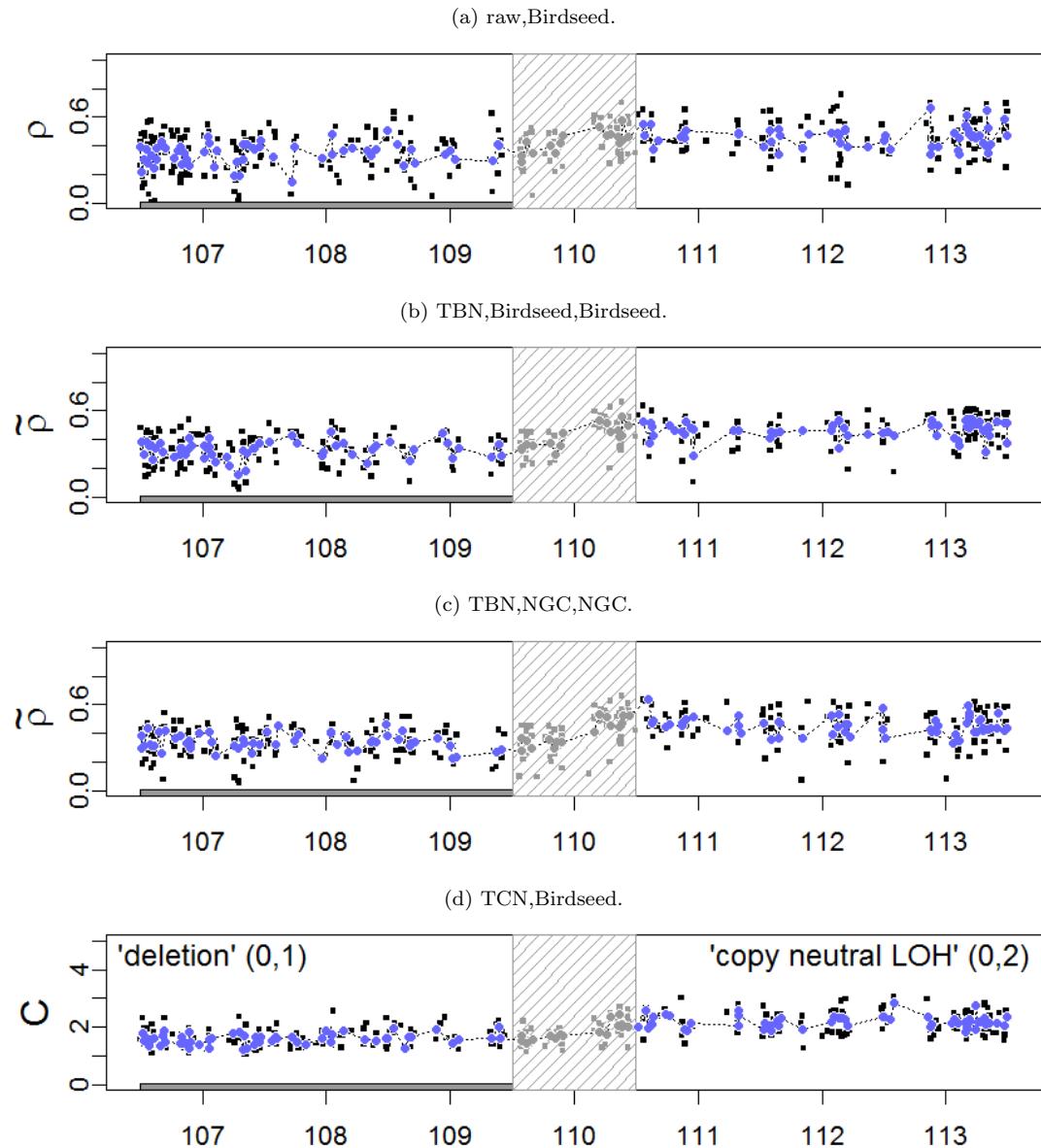


Figure 28: Decrease in Heterozygosity (DH) and total copy numbers for region TCGA-23-1027:Chr10@106.5-113.5,cp=110+/-0.5,s=2/3. Only heterozygous SNPs are plotted. There are 219 loci of state 'deletion' (0,1) ("negatives") and 219 loci of state 'copy neutral LOH' (0,2) ("positives"), where the latter are highlighted with a solid bar beneath. In total 64 loci within the safety margin were excluded.

## 6.2 Allele B fraction density plots

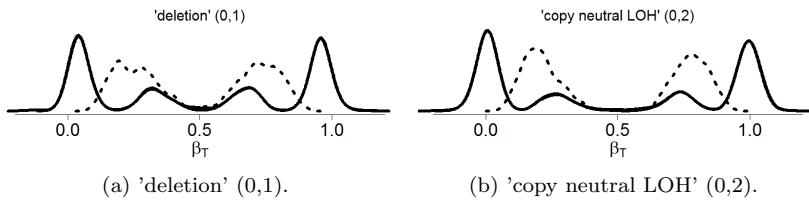


Figure 29: Density of raw (dashed lines) and TumorBoost-normalized (solid lines) allele B fractions for region TCGA-23-1027:Chr10@106.5-113.5, cp=110+/-0.5, s=2/3.

## 6.3 ROC curves

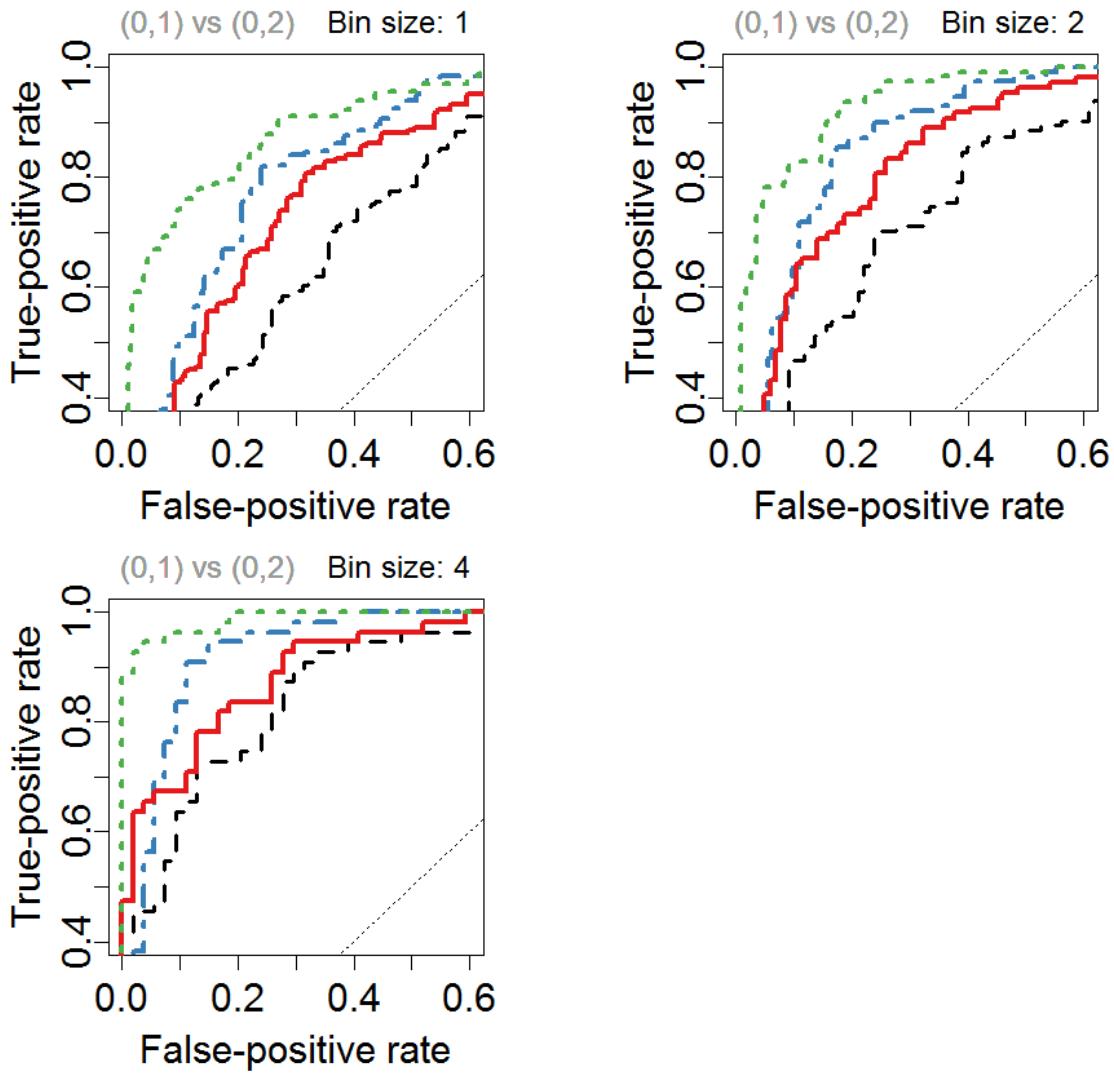


Figure 30: ROC curves for each preprocessing method at the full resolution as well as 2 different amounts of smoothing (using the mean() function) for region TCGA-23-1027:Chr10@106.5-113.5, cp=110+/-0.5, s=2/3. Legend: raw,Birdseed (dashed; #000000), TBN,Birdseed,Birdseed (dash-dotted; #377EB8), TBN,NGC,NGC (solid; #E41A1C) and TCN,Birdseed (dotted; #4DAF4A).

## 6.4 $(\beta_N, \beta_T)$ plots

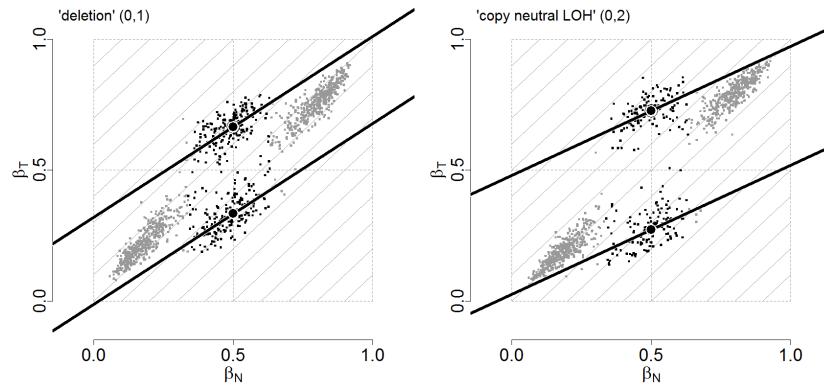


Figure 31: raw,NGC for region TCGA-23-1027:Chr10@106.5-113.5,cp=110+/-0.5,s=2/3.

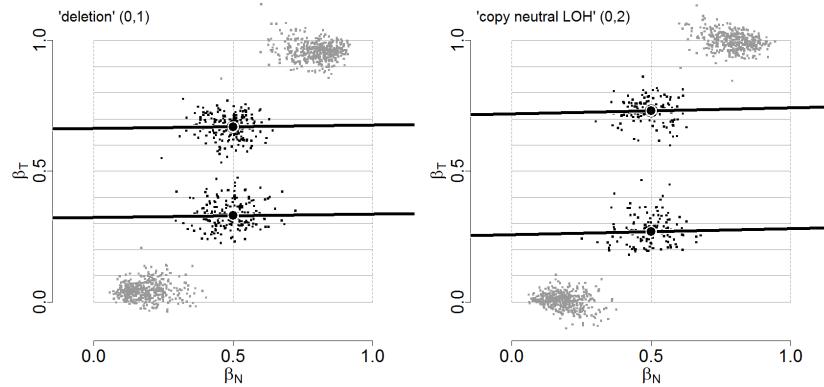


Figure 32: TBN,Birdseed,Birdseed for region TCGA-23-1027:Chr10@106.5-113.5,cp=110+/-0.5,s=2/3.

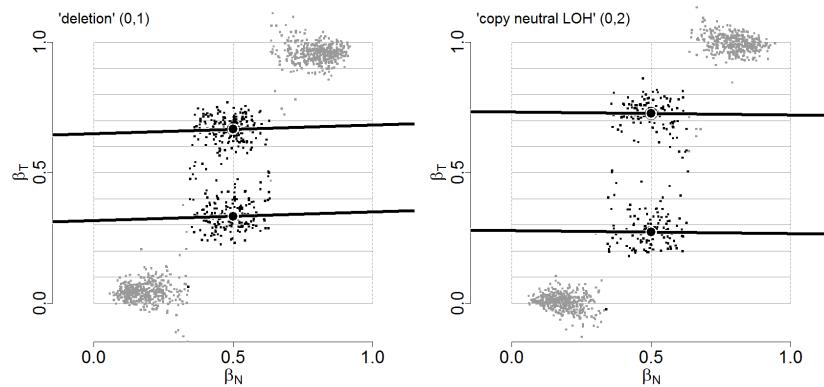


Figure 33: TBN,NGC,NGC for region TCGA-23-1027:Chr10@106.5-113.5,cp=110+/-0.5,s=2/3.

## 6.5 Allele-specific copy number estimates

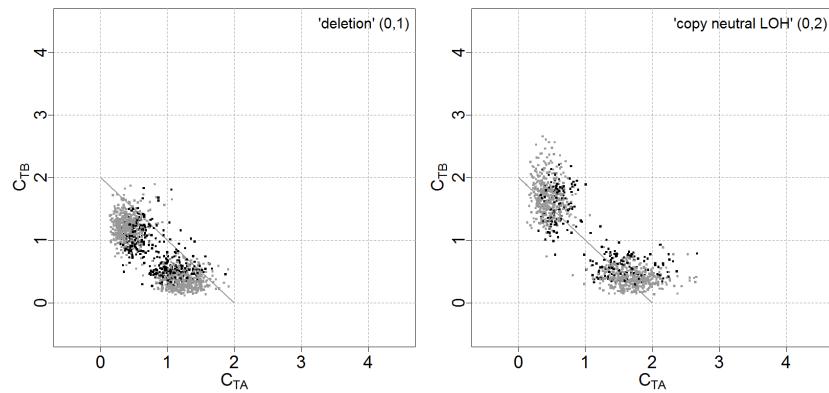


Figure 34: raw,NGC for region TCGA-23-1027:Chr10@106.5-113.5,cp=110+/-0.5,s=2/3.

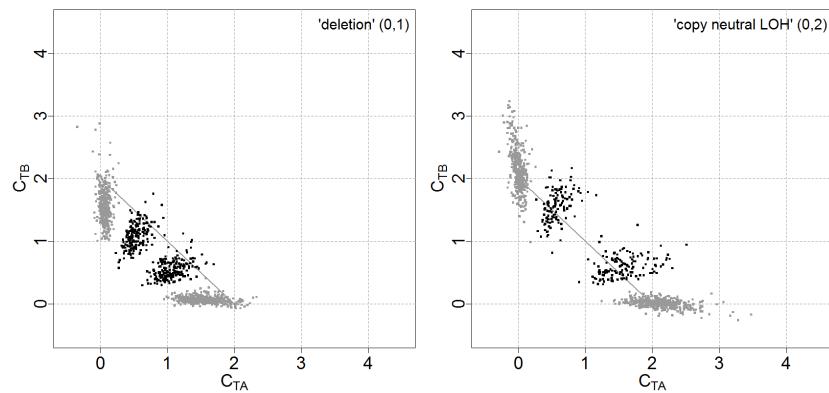


Figure 35: TBN,Birdseed,Birdseed for region TCGA-23-1027:Chr10@106.5-113.5,cp=110+/-0.5,s=2/3.

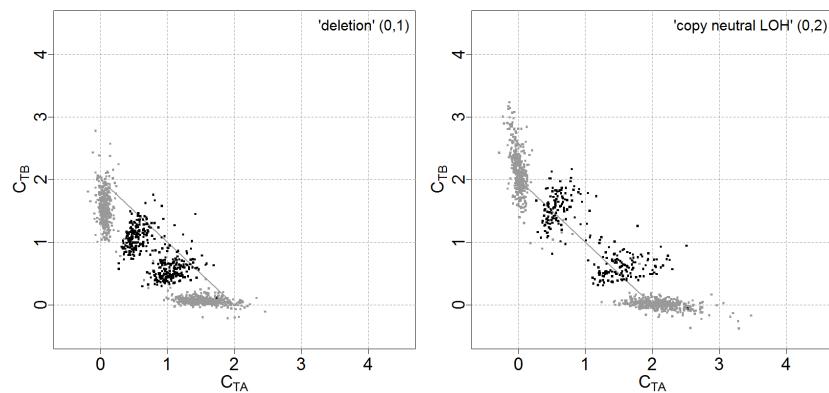


Figure 36: TBN,NGC,NGC for region TCGA-23-1027:Chr10@106.5-113.5,cp=110+/-0.5,s=2/3.

## 7 Region: TCGA-23-1027:Chr2@55-75.0,cp=65.0+/-0.5,s=0/1

### 7.1 Decrease in Heterozygosity (DH) and total copy-number tracks

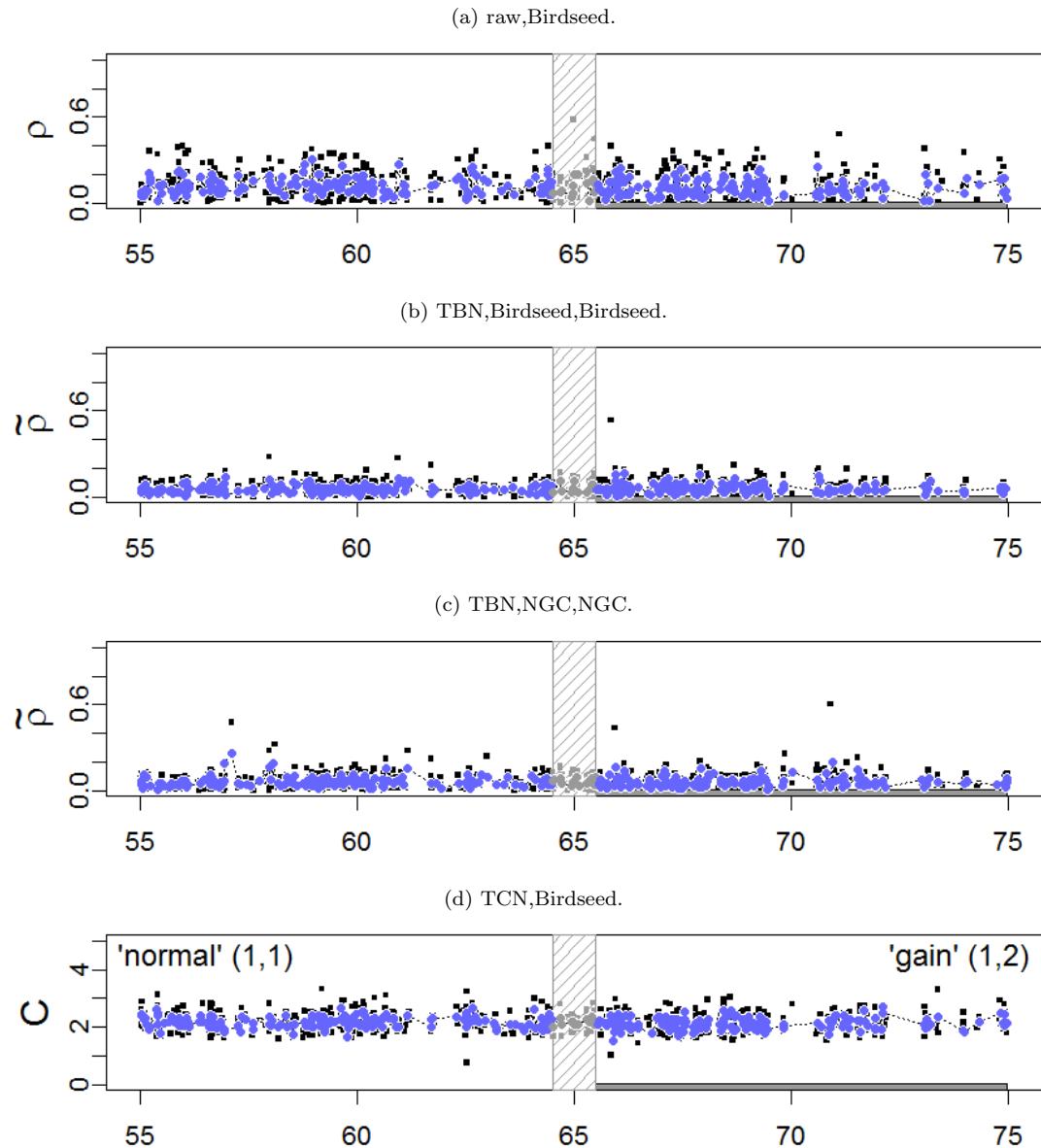


Figure 37: Decrease in Heterozygosity (DH) and total copy numbers for region TCGA-23-1027:Chr2@55-75.0,cp=65.0+/-0.5,s=0/1. Only heterozygous SNPs are plotted. There are 644 loci of state 'normal' (1,1) ("negatives") and 644 loci of state 'gain' (1,2) ("positives"), where the latter are highlighted with a solid bar beneath. In total 54 loci within the safety margin were excluded.

## 7.2 Allele B fraction density plots

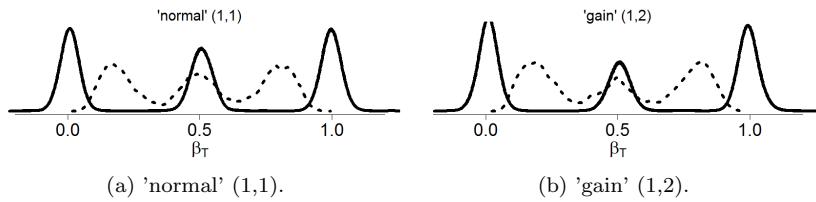


Figure 38: Density of raw (dashed lines) and TumorBoost-normalized (solid lines) allele B fractions for region TCGA-23-1027:Chr2@55-75.0,cp=65.0+/-0.5,s=0/1.

## 7.3 ROC curves

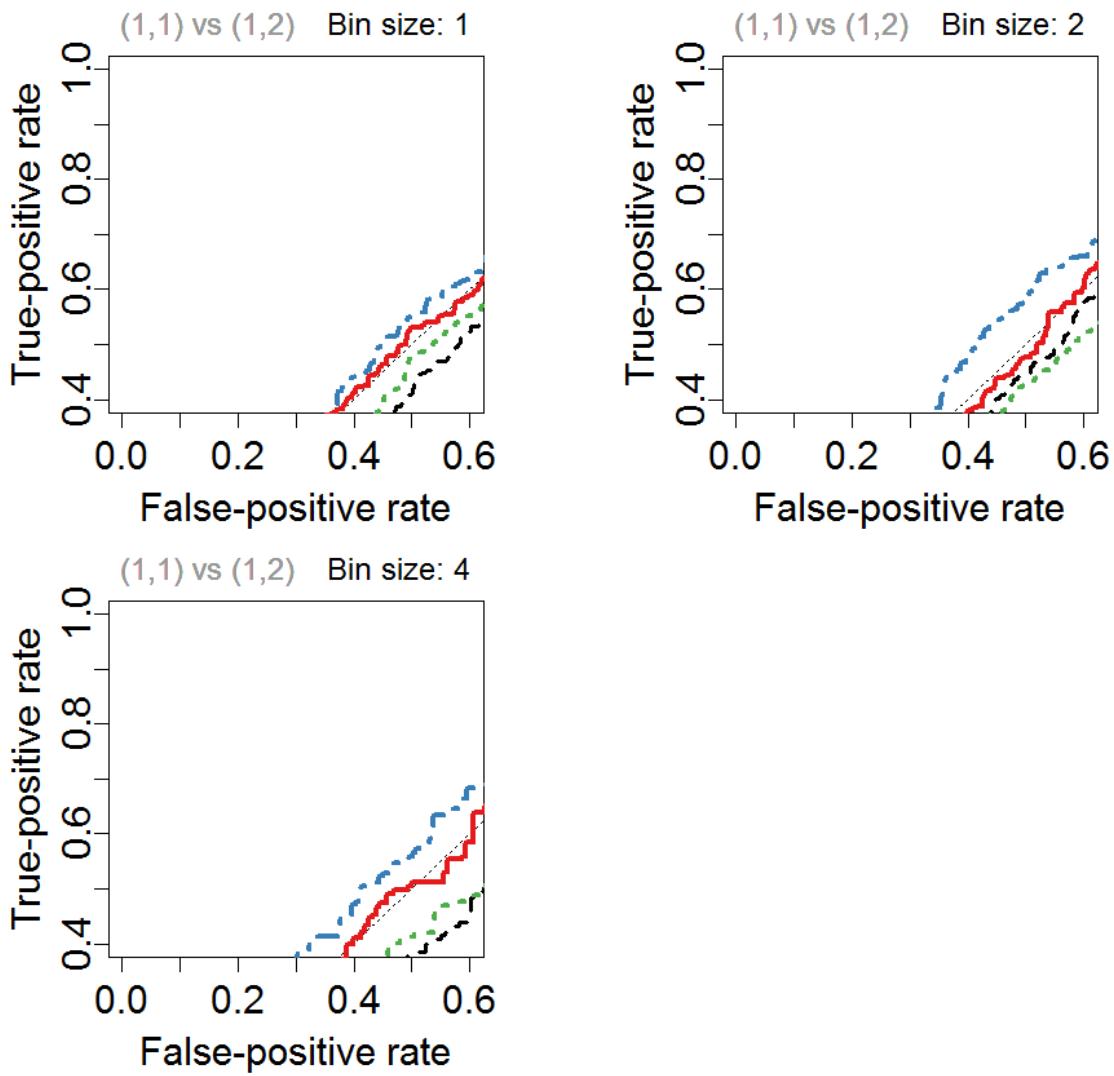


Figure 39: ROC curves for each preprocessing method at the full resolution as well as 2 different amounts of smoothing (using the `mean()` function) for region TCGA-23-1027:Chr2@55-75.0,cp=65.0+/-0.5,s=0/1. Legend: raw,Birdseed (dashed; `#000000`), TBN,Birdseed,Birdseed (dash-dotted; `#377EB8`), TBN,NGC,NGC (solid; `#E41A1C`) and TCN,Birdseed (dotted; `#4DAF4A`).

## 7.4 $(\beta_N, \beta_T)$ plots

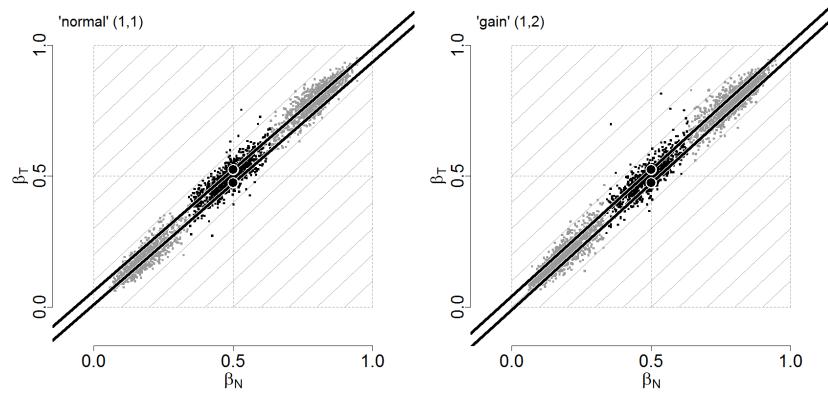


Figure 40: raw,NGC for region TCGA-23-1027:Chr2@55-75.0,cp=65.0+/-0.5,s=0/1.

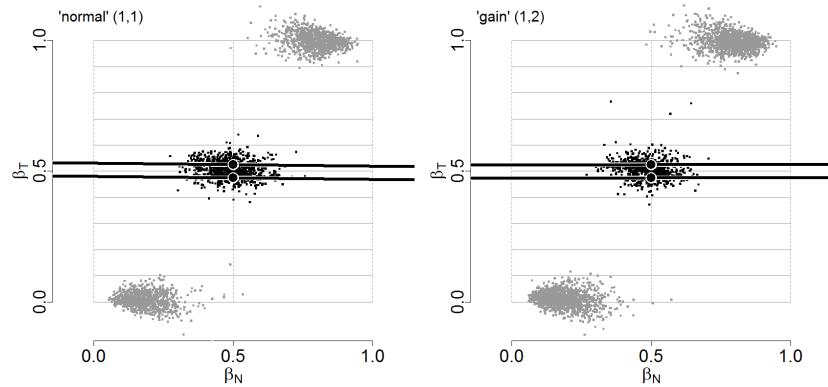


Figure 41: TBN,Birdseed,Birdseed for region TCGA-23-1027:Chr2@55-75.0,cp=65.0+/-0.5,s=0/1.

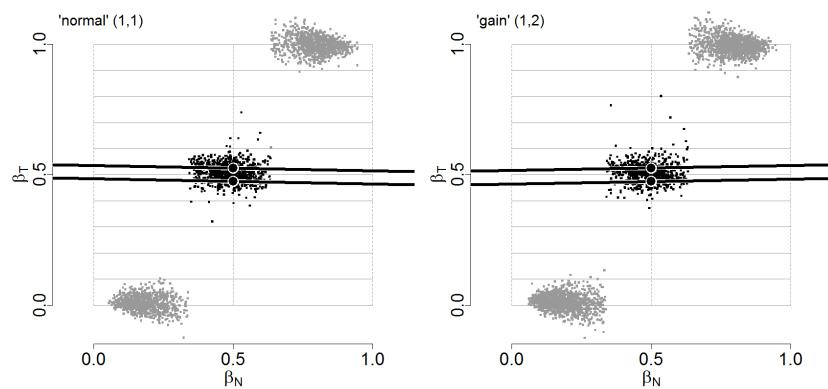


Figure 42: TBN,NGC,NGC for region TCGA-23-1027:Chr2@55-75.0,cp=65.0+/-0.5,s=0/1.

## 7.5 Allele-specific copy number estimates

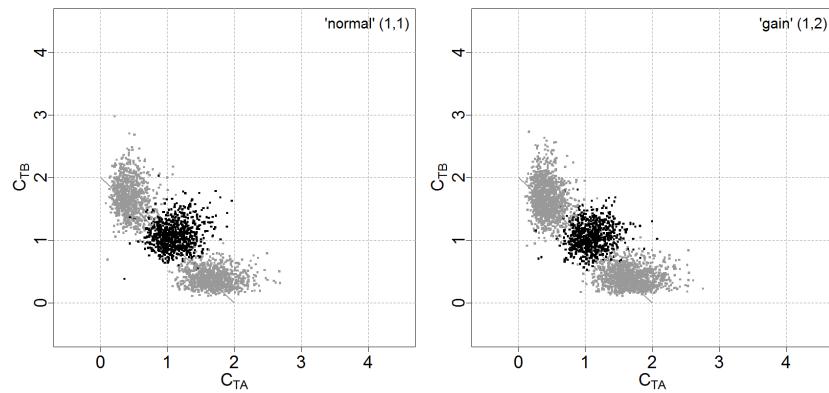


Figure 43: raw,NGC for region TCGA-23-1027:Chr2@55-75.0,cp=65.0+/-0.5,s=0/1.

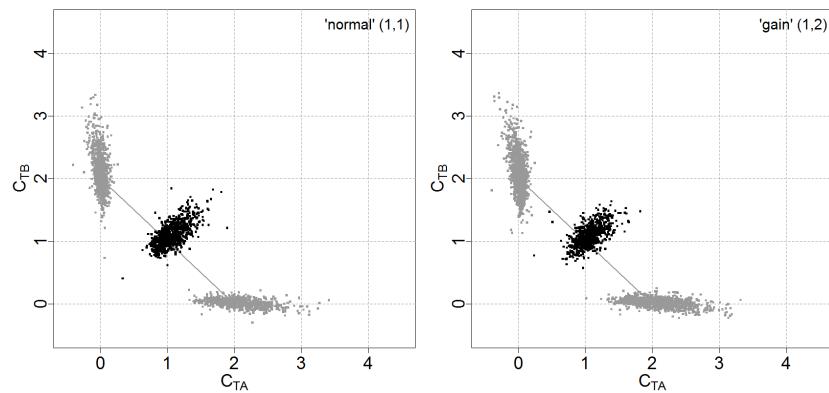


Figure 44: TBN,Birdseed,Birdseed for region TCGA-23-1027:Chr2@55-75.0,cp=65.0+/-0.5,s=0/1.

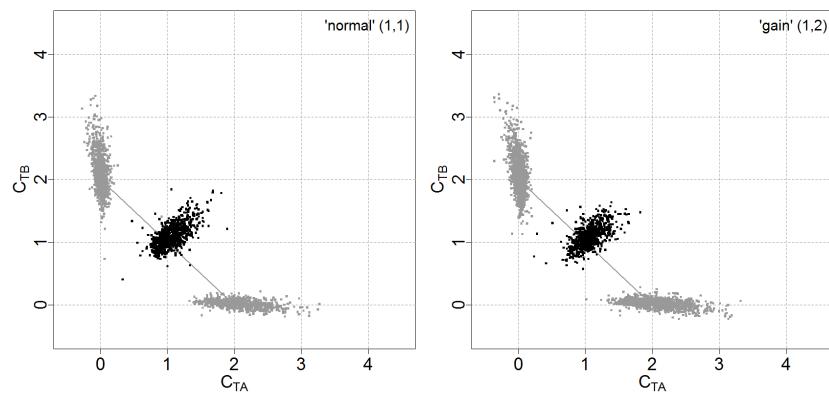


Figure 45: TBN,NGC,NGC for region TCGA-23-1027:Chr2@55-75.0,cp=65.0+/-0.5,s=0/1.

## 8 Bootstrap estimates of test statistics for all regions

	0/1	1/3	0/2	2/3	0/1
raw,Birdseed	6.071±1.020	24.955±1.496	20.961±1.418	9.765±0.946	1.024±0.790
TBN,Birdseed,Birdseed	20.775±1.235	39.297±1.805	40.133±2.575	13.892±1.138	0.856±0.591
TBN,NGC,NGC	19.508±1.354	34.120±1.960	36.493±2.121	12.000±1.054	0.821±0.627
TCN,Birdseed	14.233±1.004	16.817±1.093	22.669±1.190	17.707±1.085	1.518±0.844

Table 2: Student test statistics of the null hypothesis of equal mean before and after each PCN change point (heterozygous SNPs): raw or TumorBoost-normalized DH, and total copy number (last line). Mean ± standard deviation across 100 samplings of 225 points (for each PCN state) from the original data set. The larger value, the more different the true means are.

## References

- Korn, J. M., Kuruvilla, F. G., McCarroll, S. A., Wysoker, A., Nemesh, J., Cawley, S., Hubbell, E., Veitch, J., Collins, P. J., Darvishi, K., Lee, C., Nizzari, M. M., Gabriel, S. B., Purcell, S., Daly, M. J., and Altshuler, D. (2008). Integrated genotype calling and association analysis of SNPs, common copy number polymorphisms and rare CNVs. *Nature Genet.*, **40**(10), 1253–1260.

## A Data files

### A.1 Total copy numbers

```
$'TCGA,OV,Birdseed,ismpolish'  
AromaUnitTotalCnBinarySet:  
Name: TCGA  
Tags: OV,Birdseed,ismpolish  
Full name: TCGA,OV,Birdseed,ismpolish  
Number of files: 1  
Names: TCGA-23-1027  
Path (to the first file): rawCnData/TCGA,OV,Birdseed,ismpolish/GenomeWideSNP`6  
Total file size: 7.08 MB  
RAM: 0.00MB
```

### A.2 Allele B fractions

```
$raw  
AromaUnitFracBCnBinarySet:  
Name: TCGA  
Tags: OV,Birdseed,ismpolish  
Full name: TCGA,OV,Birdseed,ismpolish  
Number of files: 1  
Names: TCGA-23-1027  
Path (to the first file): totalAndFracBData/TCGA,OV,Birdseed,ismpolish/GenomeWideSNP`6  
Total file size: 7.08 MB  
RAM: 0.00MB  
  
$'TBN,Birdseed'  
AromaUnitFracBCnBinarySet:  
Name: TCGA  
Tags: OV,Birdseed,ismpolish,TBN,Birdseed  
Full name: TCGA,OV,Birdseed,ismpolish,TBN,Birdseed  
Number of files: 1  
Names: TCGA-23-1027  
Path (to the first file): totalAndFracBData/TCGA,OV,Birdseed,ismpolish,TBN,Birdseed/GenomeWideSNP`6  
Total file size: 7.08 MB  
RAM: 0.00MB
```

```
$'TBN,NGC'  
AromaUnitFracBCnBinarySet:  
Name: TCGA  
Tags: OV,Birdseed,ismpolish,TBN,NGC  
Full name: TCGA,OV,Birdseed,ismpolish,TBN,NGC  
Number of files: 1  
Names: TCGA-23-1027  
Path (to the first file): totalAndFracBData/TCGA,OV,Birdseed,ismpolish,TBN,NGC/GenomeWideSNP`6  
Total file size: 7.08 MB  
RAM: 0.00MB
```

### A.3 Genotype calls

```
$Birdseed  
AromaUnitGenotypeCallSet:  
Name: TCGA  
Tags: OV,Birdseed,ismpolish,Birdseed  
Full name: TCGA,OV,Birdseed,ismpolish,Birdseed  
Number of files: 1  
Names: TCGA-23-1027
```

Path (to the first file): callData/TCGA,OV,Birdseed,ismpolish,Birdseed/GenomeWideSNP`6  
Total file size: 3.54 MB  
RAM: 0.00MB

\$NGC  
AromaUnitGenotypeCallSet:  
Name: TCGA  
Tags: OV,Birdseed,ismpolish,NGC  
Full name: TCGA,OV,Birdseed,ismpolish,NGC  
Number of files: 1  
Names: TCGA-23-1027  
Path (to the first file): callData/TCGA,OV,Birdseed,ismpolish,NGC/GenomeWideSNP`6  
Total file size: 3.54 MB  
RAM: 0.00MB

#### A.4 Genotype confidence scores

\$Birdseed  
AromaUnitSignalBinarySet:  
Name: TCGA  
Tags: OV,Birdseed,ismpolish,Birdseed  
Full name: TCGA,OV,Birdseed,ismpolish,Birdseed  
Number of files: 1  
Names: TCGA-23-1027  
Path (to the first file): callData/TCGA,OV,Birdseed,ismpolish,Birdseed/GenomeWideSNP`6  
Total file size: 7.08 MB  
RAM: 0.00MB

\$NGC  
AromaUnitSignalBinarySet:  
Name: TCGA  
Tags: OV,Birdseed,ismpolish,NGC  
Full name: TCGA,OV,Birdseed,ismpolish,NGC  
Number of files: 1  
Names: TCGA-23-1027  
Path (to the first file): callData/TCGA,OV,Birdseed,ismpolish,NGC/GenomeWideSNP`6  
Total file size: 7.08 MB  
RAM: 0.00MB

## B Session information

This report was automatically generated using the R.rsp package.

- R version 2.10.0 Patched (2009-11-21 r50532), i386-pc-mingw32
- Locale: LC\_COLLATE=English\_United States.1252, LC\_CTYPE=English\_United States.1252, LC\_MONETARY=English\_United States.1252, LC\_NUMERIC=C, LC\_TIME=English\_United States.1252
- Base packages: base, datasets, graphics, grDevices, methods, stats, utils
- Other packages: aroma.cn.eval 0.1.1, aroma.core 1.3.5, aroma.light 1.15.1, digest 0.4.1, MASS 7.3-3, matrixStats 0.1.8, R.cache 0.2.0, R.filesets 0.6.5, R.menu 0.0.5, R.methodsS3 1.1.0, R.oo 1.6.6, R.rsp 0.3.6, R.utils 1.2.4, RColorBrewer 1.0-2, xtable 1.5-5
- Loaded via a namespace (and not attached): affxparser 1.18.0